Kırım-Kongo Kanamalı Ateşi

Prof. Dr. Nazif ELALDI

Cumhuriyet Üniversitesi, Sivas, TR

nelaldi61@yahoo.com

Viral Kanamalı Ateş

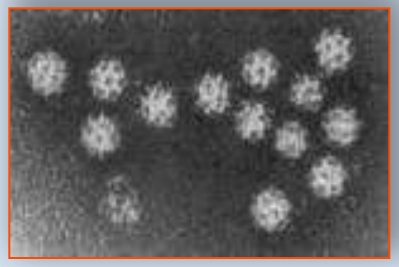
Ateş

Kanamalar

Viral Kanamalı Ateş Etkenleri

- ***Filoviridae***
  - Marburg virus and Ebola virus
- ***Arenaviridae***
  - Lassa virus
    Guanarito virus
- ***Bunyaviridae***
  - CCHFV, RVFV ve Hanta
- ***Flaviviridae***
  - Yellow fever virus, Dengue virus ve Alkhumra virus

14 farklı etken !



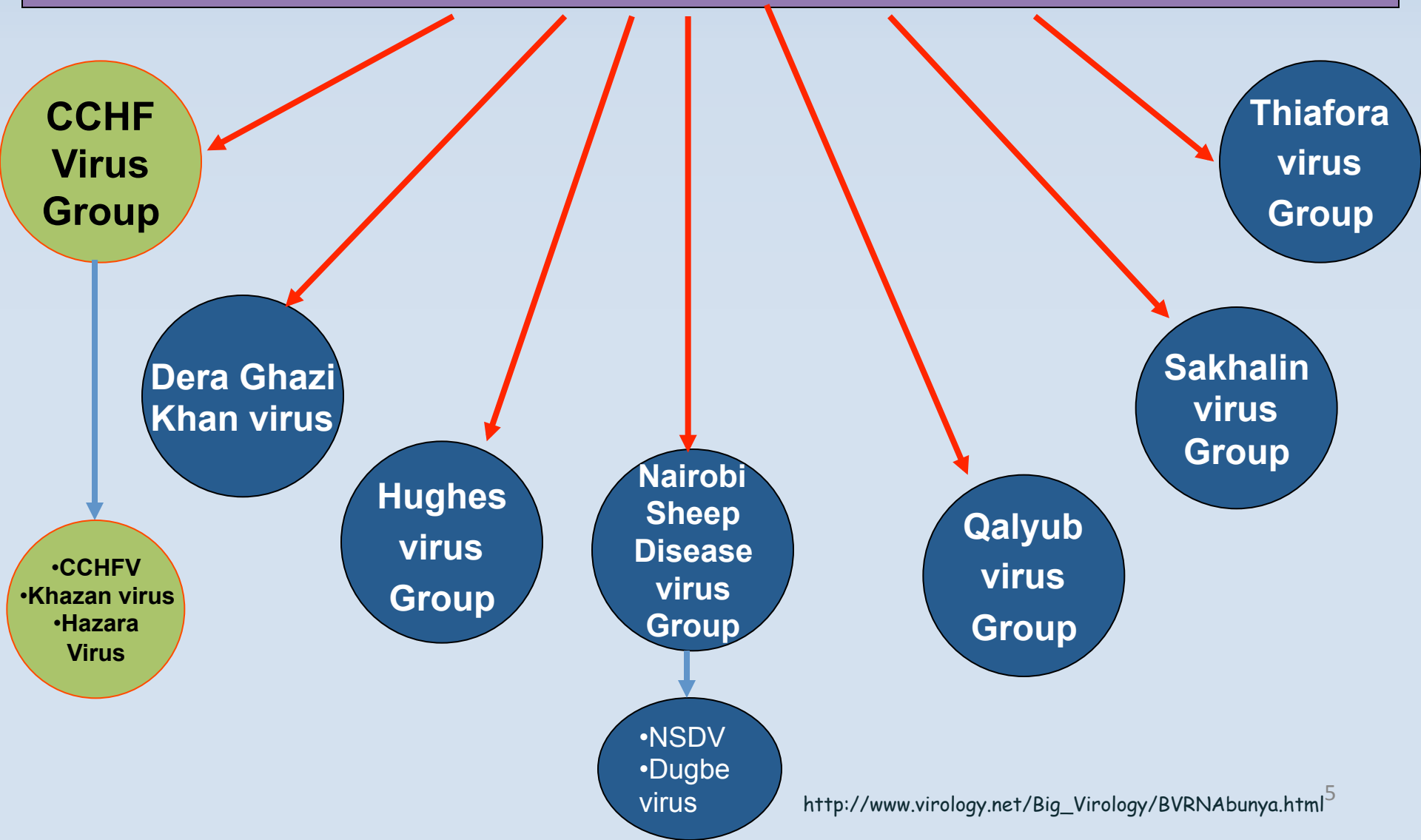
BUNYAVIRIDAE

350 civarı virüs !

- Bunyavirus
- Hantavirus
- [illegible]ovirus
- Phlebovirus
- Tospovirus

* http://www.virology.net/Big_Virology/BVRNAbunya.html

Nairovirus (7 alt cins içerir)



http://www.virology.net/Big_Virology/BVRNAbunya.html

Virüs sayısı artıyor !

Kupe Virus, a New Virus in the Family *Bunyaviridae*, Genus *Nairovirus*, Kenya

Mary B. Crabtree, Rosemary Sang, and Barry R. Miller

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 2, February 2009

We have previously described isolation and preliminary identification of a virus related to Dugbe virus (DUGV), family *Bunyaviridae*, genus *Nairovirus*. Six isolates of the virus were obtained from pools of *Amblyomma gemma* and *Rhipicephalus pulchellus* ticks collected from hides of cattle in Nairobi, Kenya, in October 1999. We report results of further characterization of this virus, including growth kinet-

genus. CCHFV, which ranges from sub-Saharan Africa to western People's Republic of China, is currently the most well characterized member of the genus. DUGV, also well characterized, is commonly isolated in surveillance studies conducted in Africa and appears to be endemic in most of the drier parts of this continent. DUGV is transmitted by ticks to vertebrates, including humans, and causes a mild

Erve virüs (Yeni Nairovirüs)

Genetic characterization of Erve virus, a European Nairovirus distantly related to Crimean-Congo hemorrhagic fever virus

Meik Dilcher · Andrea Koch · Lekbira Hasib · Gerhard Dobler · Frank T. Hufert · Manfred Weidmann

Virus Genes (2012) 45:426–432
DOI 10.1007/s11262-012-0796-8

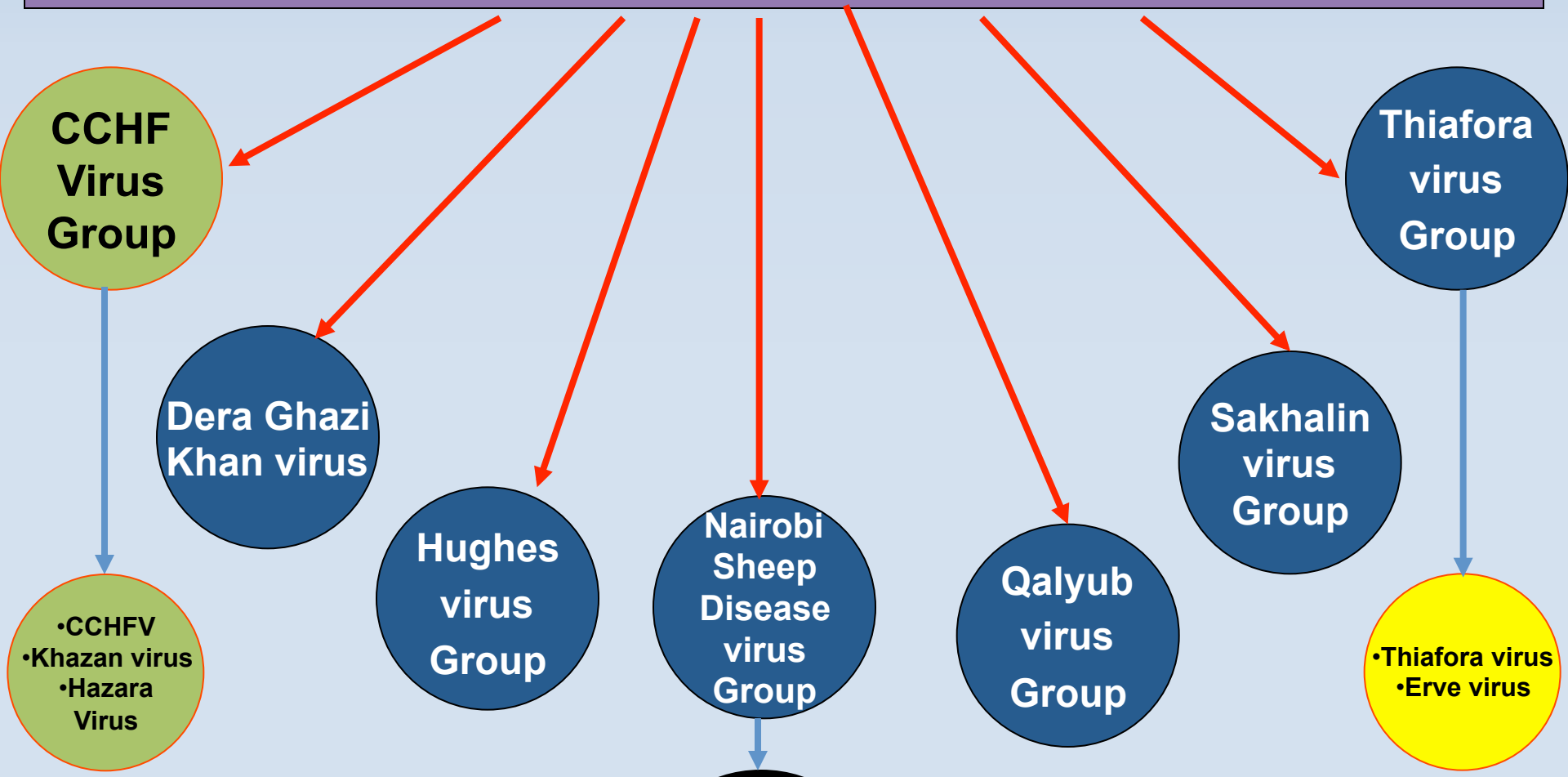
Received: 17 April 2012 / Accepted: 20 July 2012 / Published online: 3 August 2012

Abstract Erve virus (ERVEV) is a European Nairovirus that is suspected to cause severe headache (thunderclap headache) and intracerebral hemorrhage. The mode of transmission to humans (ticks or mosquitoes) is still unknown. Currently, no standardized testing method for

Introduction

Erve virus (ERVEV) was isolated in 1982 from tissues of a white-toothed shrew (*Crocidura russula*) collected in the Erve River Valley in northwestern France after intracerebral

Nairovirus (7 alt cins içerir)



En az 35 virüs var!

http://www.virology.net/Big_Virology/BVRNAbunya.html

SFTS virus (Yeni Phlebovirus)

ORIGINAL ARTICLE

Fever with Thrombocytopenia Associated with a Novel Bunyavirus in China

Xue-Jie Yu, M.D., Ph.D., Mi-Fang Liang, M.D., Shou-Yin Zhang, Ph.D.,*
Yan Liu, M.D., Jian-Dong Li, Ph.D., Yu-Lan Sun, M.D., Lihong Zhang M.D.,
Quan-Fu Zhang, B.Sc., Vsevolod L. Popov, Ph.D., Chuan Li, B.Sc., Jing Qu, B.Sc.,
Qun Li, M.D., Yan-Ping Zhang, M.D., Rong Hai, M.D., Wei Wu, M.Sc.,
Qin Wang, Ph.D., Fa-Xian Zhan, Ph.D., Xian-Jun Wang, M.D., Biao Kan, Ph.D.,
Shi-Wen Wang, Ph.D., Kang-Lin Wan, Ph.D., Huai-Qi Jing, M.D.,
Jin-Xin Lu, M.D., Wen-Wu Yin, M.Ph., Hang Zhou, M.S, Xu-Hua Guan, Ph.D.,
Jia-Fa Liu, M.D., Zhen-Qiang Bi, Ph.D., Guo-Hua Liu, M.D., Jun Ren, M.D.,
Hua Wang, M.D., Zhuo Zhao, M.D., Jing-Dong Song, M.Sc., Jin-Rong He, B.Sc.,
Tao Wan, Ph.D., Jing-Shan Zhang, M.S., Xiu-Ping Fu, M.S., Li-Na Sun, Ph.D.,
Xiao-Ping Dong, Ph.D., Zi-Jian Feng, M.D., Wei-Zhong Yang, M.D., Tao Hong, M.D.,
Yu Zhang, M.D., David H. Walker, M.D., Yu Wang, M.D., Ph.D., and De-Xin Li, M.D.

ABSTRACT

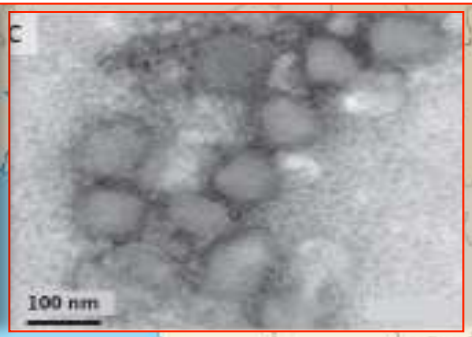
BACKGROUND

Heightened surveillance of acute febrile illness in China since 2009 has led to the identification of a severe fever with thrombocytopenia syndrome (SFTS) with an unknown cause. Infection with *Anaplasma phagocytophilum* has been suggested as a cause,

N ENGL J MED 364;16 NEJM.ORG APRIL 21, 2011

SFTS virüs, Çin, 2009

- **Çinde 6 Eyalette 171 olgu**
- **Mortalite, %12**
  - Ateş
  - Trombositopeni
  - Lökopeni
  - Multiple Organ Yetmezliği
- ***Haemaphysalis longicornis***
  (Biyolojik vektör kene)



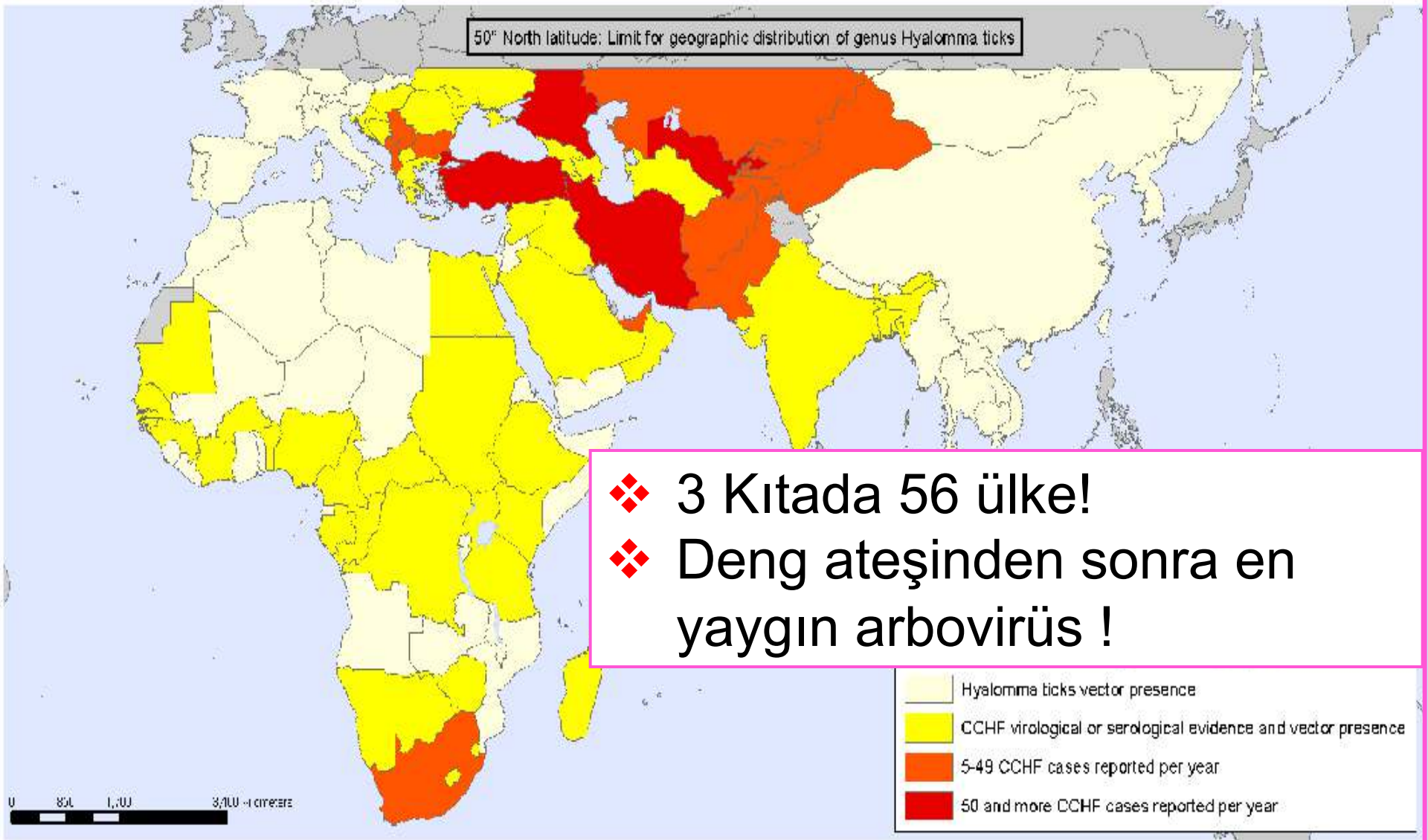
N ENGL J MED 364;16 NEJM.ORG APRIL 21, 2011

BUNYAVIRIDAE

- Bunyavirus
- Hantavirus
- Nairovirus
- Phlebovirus
  - STFS virus
- Tospovirus

* http://www.virology.net/Big_Virology/BVRNAbunya.html

Geographic distribution of Crimean-Congo Haemorrhagic Fever



- 3 Kıtada 56 ülke!
- Deng ateşinden sonra en yaygın arbovirüs !

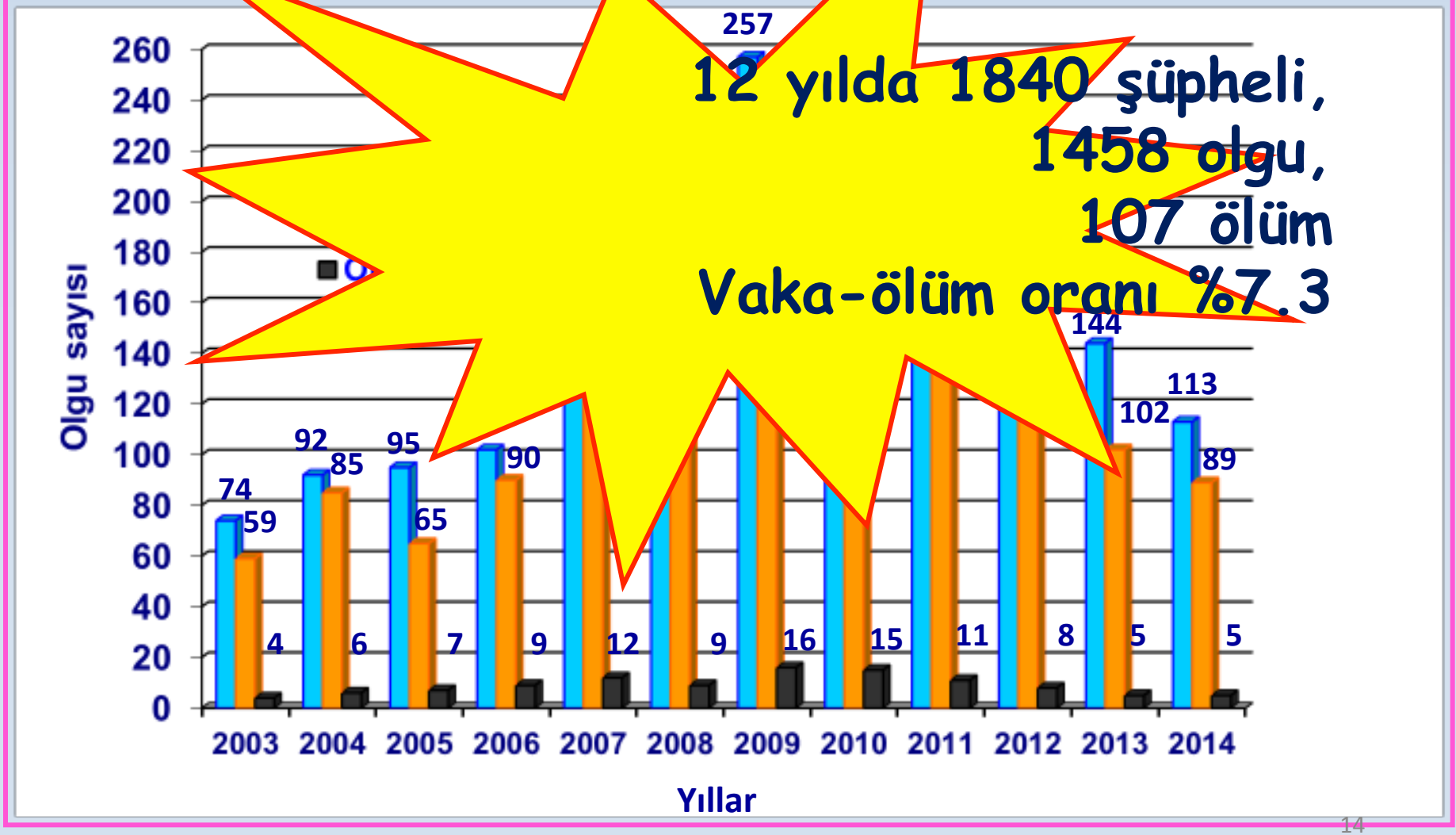
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

KKKA Olgu ve Ölümleri Dağılımı (Türkiye 2002-2014)

KKKA Olgu ve Ölümleri Dağılımı (CÜTF-Enf Hast AD, 2002-2014)



KKKA bulaş yolları

- İnfekte kene yapışması/kene kırma
- Viremik hayvanlar
  - Hayvana ait kan ve dokulara temas
  - İnfekte hastalardan (hastanede, toplumd
  - Direkt temas
  - İnfekte doku ve kan teması ile
  - Anneden bebeğe (vertikal bulaş)
  - Laboratuvardan direkt temas ile/havadan (?)
  - Hava yolu?

KKKA için risk gurupları

- Endemik bölgede yaşayan/ziyaretçi
- Çiftçiler
- Hayvancılık yapanlar
- Kasaplar, mezbaha çalışanları
- Veteriner hekimler
- Sağlık personeli
- Laboratuvar çalışanları
- Hasta yakınları

Hamilelikte KKKA

Novel Insights from Clinical Practice

Gynecologic and Obstetric Investigation

Gynecol Obstet Invest 2014;77:266–271
DOI: 10.1159/000360699

Received: August 14, 2013
Accepted after revision: February 17, 2014
Published online: April 12, 2014

Favorable Outcomes for both Mother and Baby Are Possible in Pregnant Women with Crimean-Congo Hemorrhagic Fever Disease: A Case Series and Literature Review

Mustafa Gokhan Gozel[a] Nazif Elaldi[a] Aynur Engin[a] Ozlem Bozoklu Akkar[b]
Fatih Bolat[c] Cem Celik[d]

Departments of [a]Infectious Diseases and Clinical Microbiology, [b]Obstetrics and Gynecology, [c]Pediatrics and [d]Medical Microbiology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

Gozel MG et al. Gynecol Obstet Invest 2014:266-71

Hamilelikte KKKA

- Literatürde bildirilen 24 KKKA'lı gebenin
  - 8 (%33)'i kaybedildi
  - 8(%33) abo
  - 4(%16) be
- 5 gebe Cumhu yet ve esi ne takip edildi
  - Hiçbirine ribavirin uygulanmadı
  - 5 gebe yaşıyor
  - Sadece 1 aborsiyon gözlendi

İlk trimestre f
açısından öne

Gozel MG et al. Gynecol Obstet Invest 2014:266-71

Sağlık Çalışanlarında KKKA

International Journal of Infectious Diseases 17 (2013) e1046–e1050

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Recommended precaution procedures protect healthcare workers from Crimean-Congo hemorrhagic fever virus☆

Mustafa Gokhan Gozel [a,*], Ilyas Dokmetas [a], Atifet Yasemin Oztop [b], Aynur Engin [a], Nazif Elaldi [a], Mehmet Bakir [a]

[a] Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Cumhuriyet University, 58140 Sivas, Turkey
[b] Department of Microbiology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

- 190 Sağlık personeli (57 hemşire, 47 doktor, 45 Lab. teknisyeni, 41 personel)
- Kişisel koruyucu ekipman kullanımı yüksek
- Sadece 1 hemşirede anti-CCHFV IgG pozitif

Hasta yakınlarına KKKA bulaşı

Am. J. Trop. Med. Hyg., 90(1), 2014, pp. 160–162
doi:10.4269/ajtmh.13-0306

Investigation of Crimean-Congo Hemorrhagic Fever Virus Transmission from Patients to Relatives: A Prospective Contact Tracing Study

Mustafa Gokhan Gozel,* Mehmet Bakir, Atifet Yasemin Oztop, Aynur Engin, Ilyas Dokmetas, and Nazif Elaldi

Department of Infectious Diseases and Clinical Microbiology, Cumhuriyet University Medical School, Sivas, Turkey; Department of Medical Microbiology, Cumhuriyet University Medical School, Sivas, Turkey

- KKKA pozitif akut hastalara direkt temaslı 116 akraba ileriye dönük olarak incelendi
  - Hiç birinde hastalık belirtisi oluşmadı
  - Tümünde KKKA serolojisi negatif idi

TÜBİTAK

ORIGINAL ARTICLE

Turk J Med Sci
2009; 39 (6): 829-832
© TÜBİTAK
E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-0904-49

Ayten KADANALI
Serpil EROL
Zülal ÖZKURT
Kemalettin ÖZDEN

Epidemiological risk factors for Crimean-Congo hemorrhagic fever patients

Aim: The aim of this study was to evaluate the epidemiological risk factors for Crimean-Congo hemorrhagic fever (CCHF) patients admitted to our hospitals between January 2004- December 2006.

Table 1. Epidemiological data for 63 patients with CCHF and controls.

	CCHF Patients *n* : 63, (%)	Control *n* : 50, (%)	P value
Age	46 ± 16.9	48.4 ± 20.2	0.499*
Female	31 (49.2%)	23 (46%)	0.739*
Male	32 (50.8%)	27 (54%)	0.290*
Farming	59 (93.6%)	14 (28%)	0.000*
Handled livestock	59 (93.6%)	24 (48%)	0.000*
Living in rural area	59 (93.6%)	22 (44%)	0.000*
Tick-bite	32 (50.8%)	12 (24%)	0.004*
Contact with a patient with CCHF	No	No	-
Camping	No	No	-

*by Chi-squared test.

Seroprevalence of Crimean-Congo haemorrhagic fever (CCHF) in risk groups in Tokat Province of Turkey

Saban Tekin[1*], Sener Barut[2], Ahmet Bursali[1], Gul Aydogan[1], Onem Yuce[1], Fatma Demir[3] and Beytullah Yildirim[4]

- 2006-2007 yıllarında 12 İlçeye ait köyler

Çalışma Gurupları

• Sağlık çalışanları	3/150 (%2)
• Hayvan teması olanlar	6/26 (%23)
• KKKA hastalarının yakınları	44/193 (%23)
• Kene yapışması hikayesi olanlar	11/106 (%10)
• Kontrol gurubu	11/240 (%4.6)
TOPLAM	**69/715 (%14.4)**

Erzurum'da KKKA seroprevalansı

- 2004 yılında

Çalışma Gurupları

• Sağlık çalışanları	16/80 (%20)
• Çiftçiler	19/114 (%17)
• Mezbaha işçileri	6/44 (%14)
• Veterinerler	3/12 (%25)
TOPLAM	**44/250 (%17.6)**

Ozkurt Z, et al. 17th ECCMID, Munich, 2007

Tokat ve Sivas Köylerinde KKKA seroprevalansı

Crimean-Congo Hemorrhagic Fever Virus in High-Risk Population, Turkey

Turabi Gunes, Aynur Engin, Omer Poyraz, Nazif Elaldi, Safak Kaya, Ilyas Dokmetas, Mehmet Bakir, and Ziynet Cinar

In the Tokat and Sivas provinces of Turkey, the overall Crimean-Congo hemorrhagic fever virus (CCHFV) seroprevalence was 12.8% among 782 members of a high-risk population. CCHFV seroprevalence was associated with history of tick bite or tick removal from animals, employment in animal husbandry or farming, and being >40 years of age.

± 3% and a design effect of 1. The estimated sample size required was 664, but the target sample size of high-risk persons was increased to 782. Another 100 persons who were not at high risk for CCHFV infection, but who lived in urban areas in the high-risk region and agreed to provide blood samples, were also included in the study. The study protocol was approved by the Cumhuriyet University Hospital Human Ethics Committee.

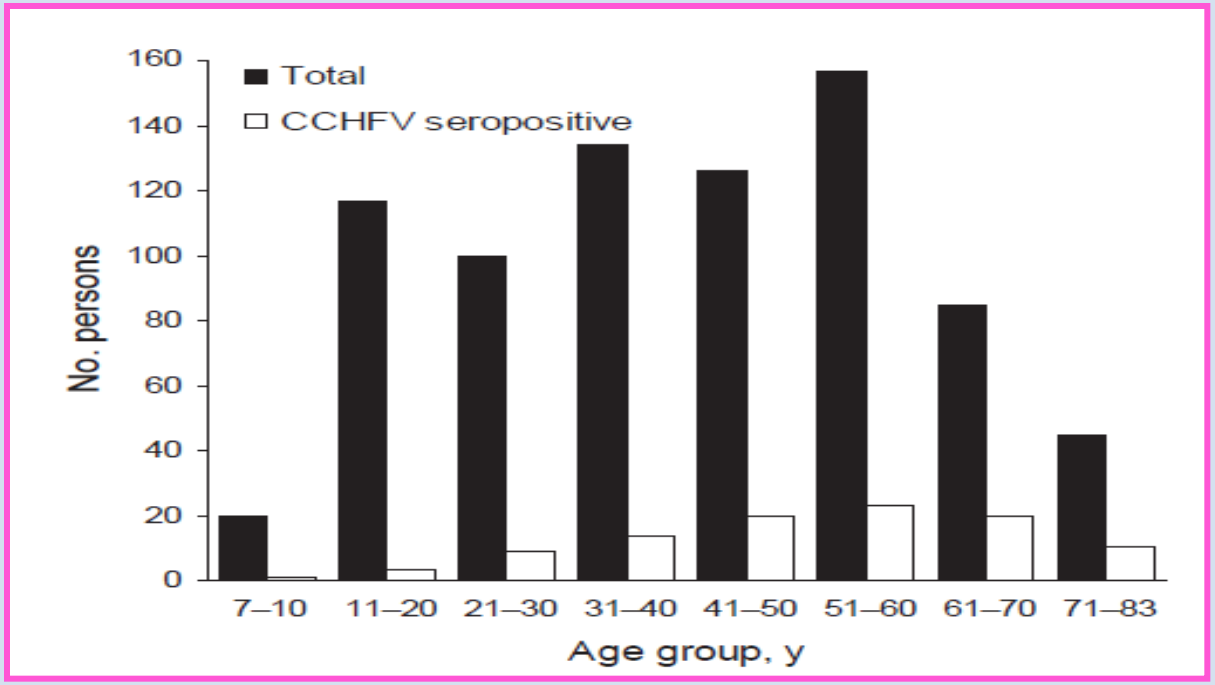
The CCHFV Seroprevalence Study Team in Turkey included a physician and a nurse who went to the selected villages and approached the heads of the village and selected families. They explained the objectives of the study and asked for written informed consent from participants or parents of participating minors and then administered an interview-based questionnaire and collected a blood sample. The questionnaire considered the following variables: age; sex; history of tick bite, tick removal from animals, animal abortion, and animal slaughtering activity; close contact with a CCHFV patient or an animal; and occupation. Blood samples (10 mL each) were collected and later tested for antibodies to CCHFV by using immunoglobulin

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 3, March 2009

- 2006 yılında Tokat ve Sivas'a ait 14 İlçede 56 köy
- Sağlık çalışanları, mezbaha işçileri, veterinerler çalışma dışı

Çalışma Gurupları

- 7 yaş ve üstü köy ahalisi 100/786 (%12.8)
- Kontrol gurubu (şehirliler) 2/100 (%2)



KKKA seroprevalansında riskler

Table 2. Demographic features and risk factors associated with CCHFV seroprevalence (univariate analysis) for persons living in rural areas of Tokat and Sivas provinces, Turkey, 2006*

Risk factor category	No. seropositive persons/total population (%)	p value
Age >40 y	73/410 (17.8)	<0.001
History of tick bite	78/483 (11.5)	0.002
Tick removal from the animals	69/450 (15.3)	0.03
Animal abortion	19/135 (14.1)	0.67
Slaughtering activity	25/151 (16.6)	0.18
Contact with CCHFV patient	14/89 (15.7)	0.44
Contact with an animal	97/734 (16.6)	0.26
Job		
Farmer	93/656 (14.2)	0.02
Animal husbandry	94/664 (14.2)	0.01
Milking	35/263 (13.3)	0.79
Student	1/38 (2.6)	0.11

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 15, No. 3, March 2009

Kelkit Vadisi'nde KKKA seroprevalansı

DISPATCHES

Subclinical Infections with Crimean-Congo Hemorrhagic Fever Virus, Turkey

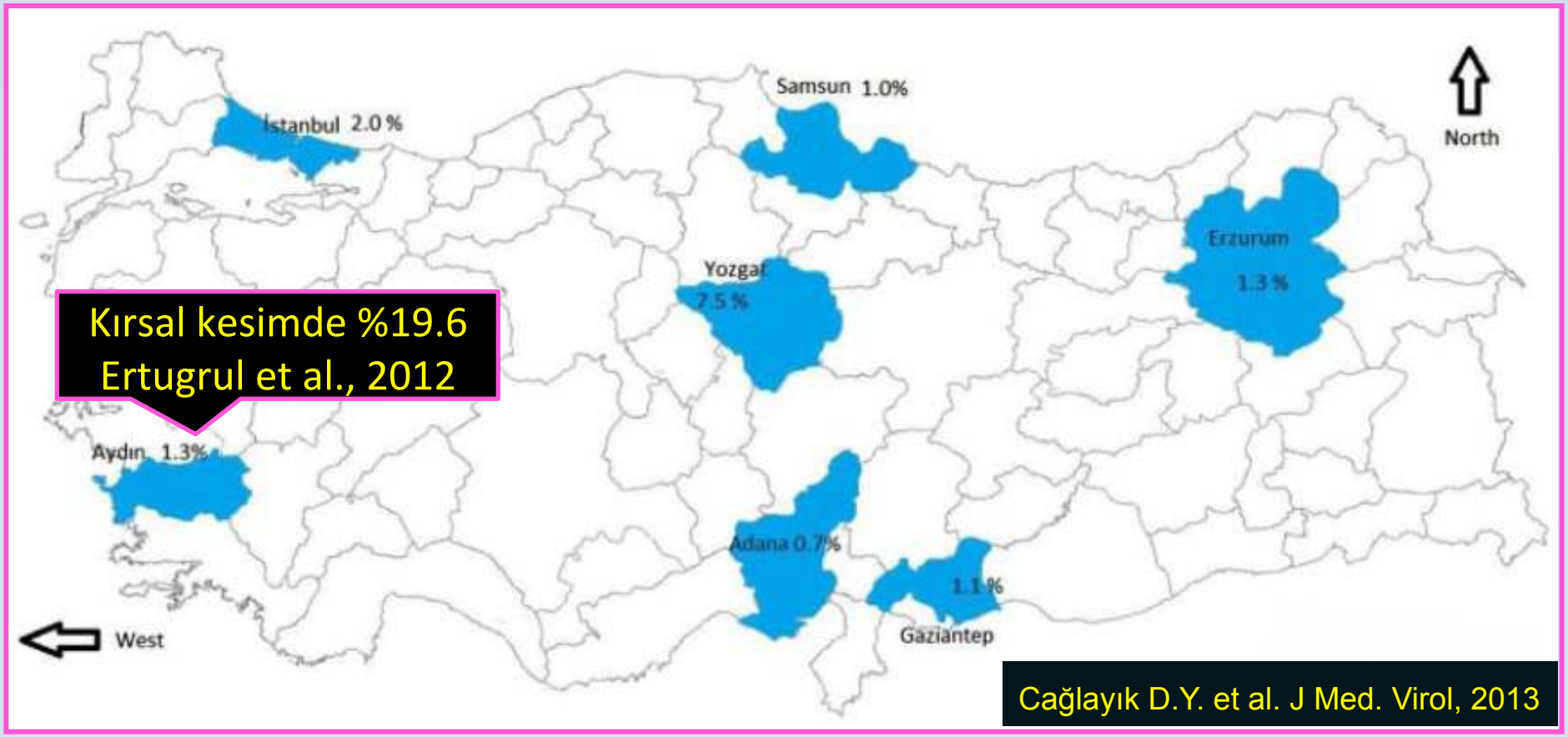
Hürrem Bodur, Esragül Akinci, Sibel Ascioglu, Pinar Öngürü, and Yavuz Uyar

Kırsal kesimde %10
2009

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 18, No. 4, April 2012

Seroprevalence and Risk Factors of Crimean–Congo Hemorrhagic Fever in Selected Seven Provinces in Turkey

- 18 yaş ve üstü sağlıklı gönüllü — 25/1066 (%2.3)
- Şehirliler — 14/796 (%1.8)
- Kırsal kesimde yaşayanlar — 11/270 (%4.1)



Ege Bölgesi'nde KKKA serolojisi

Arboviruses in the Mediterranean Countries

6th FEMS Symposium

Present Status of Arbovirus Sero-Epidemiology in the Aegean Region of Turkey

DEMIR SERTER

Department of Microbiology and Infectious Diseases, School of Medicine,
Ege University, Izmir, Turkey

Bunyavirus-like genus: Crimean Hemorrhagic Fever-Congo virus (CHF-C) was used as antigen. % 9.21 of the sera were found to contain HA-inhibiting antibodies against the antigen (Table 8). This percentage is quite high for such a tick-borne infection. This high percentage

KKKA yayılımında Göçmen kuşlar, TR

Role of Migratory Birds in Spreading Crimean-Congo Hemorrhagic Fever, Turkey

Hakan Leblebicioglu, Cafer Eroglu, Kiraz Erciyas-Yavuz, Murat Hokelek, Mustafa Acici, and Hava Yilmaz

We investigated migratory birds' role in spreading Crimean-Congo hemorrhagic fever virus (CCHFV) through attached ticks. We detected CCHFV RNA in ticks on migratory birds in Turkey. Two isolates showed similarity with CCHFV genotype 4, suggesting a role for ticks in CCHFV epidemics in Turkey and spread of CCHFV by birds.

The Study

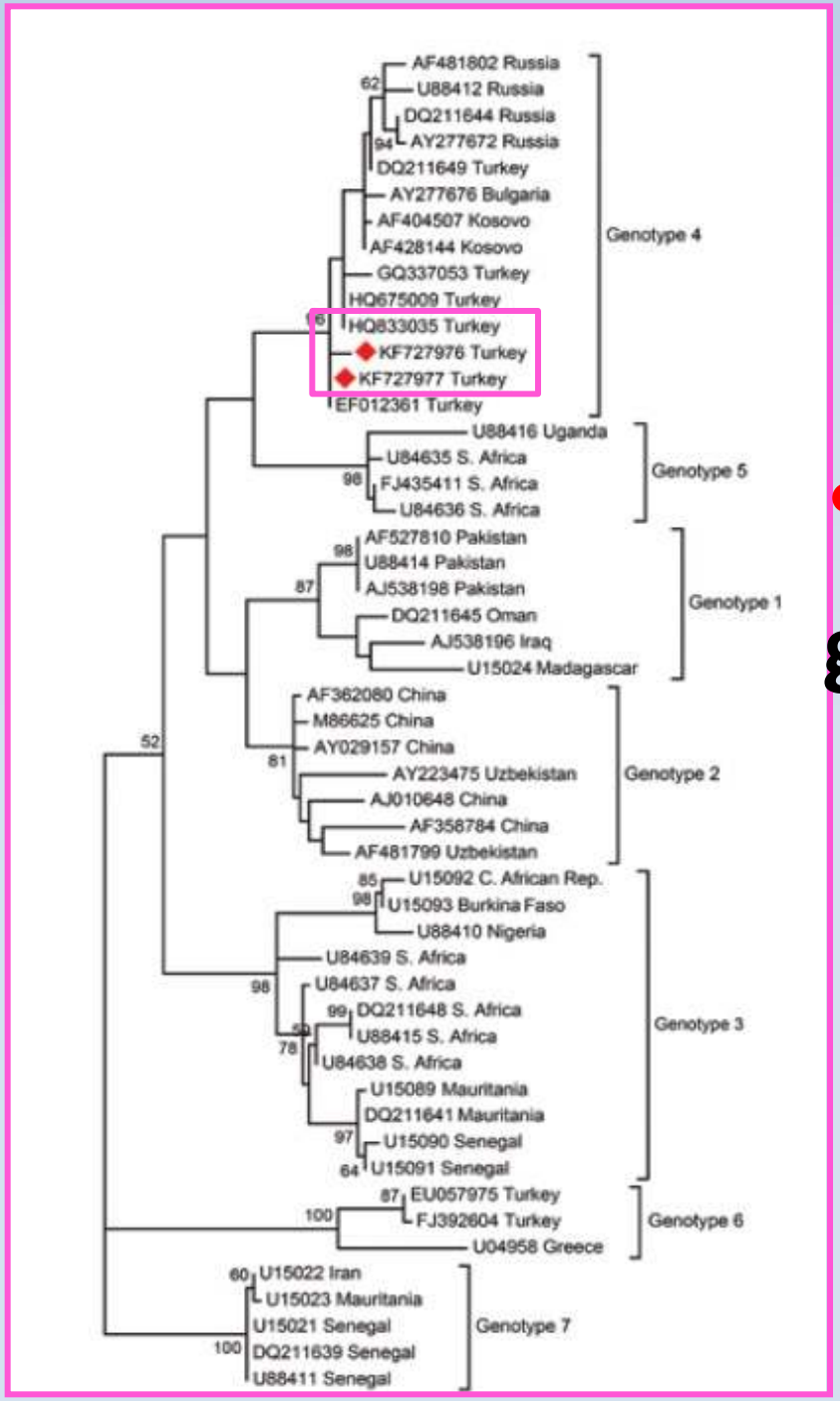
Birds were caught by mist-nets, banded (ringed), and examined for ticks at the Cernek Bird Ringing Station (41°36'N, 36°05'E) in the Kizilirmak Delta in Turkey, an internationally important wetland area for birds (*4*). We conducted the study during the spring and autumn migration seasons in 2010 and 2011 and in spring 2012. Bird species and number of ticks on each species were recorded. Each tick was speciated by examining morphologic characteristics under stereomicroscope (*5*).

The identified ticks were placed in tubes with steel beads and homogenized at the maximum speed (50 Hz) for 10 min in TissueLyser LT device (QIAGEN, Hilden, Germany). RNA was isolated according to the manufacturer's recommendations by using High Pure Viral Nucleic Acid Kit (Roche Applied Science, Mannheim, Germany), but as a small modification, the homogenized tick mixture was kept at 37°C for 1 h.

In accordance with the manufacturer's recommenda-

- 188 keneden 2'sinde PCR ile CCHFV pozitif
- Hyalomma sp. 1, Ixodes sp. 1

Leblebicioğlu H. et al. Emerg Infect Dis 2014



- **S genom segmentine göre genotip 4**

Leblebicioğlu H. et al. Emerg Infect Dis 2014

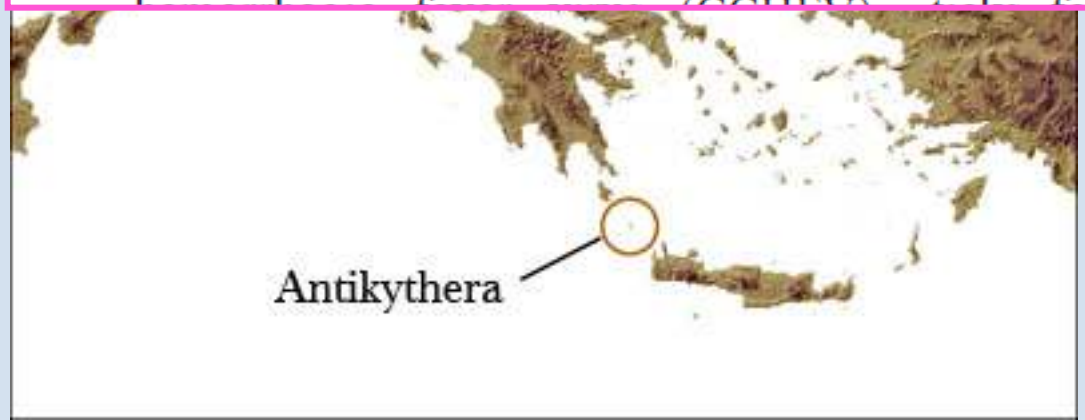
KKKA yayılımında Göçmen kuşlar, GR

Migratory Birds, Ticks, and Crimean-Congo Hemorrhagic Fever Virus

To the Editor: In a recently published study, Estrada-Peña et al. reported the finding of Crimean-Congo

stricto (s.s.), i.e., the principal vectors of CCHFV (*2*). Of 10 morphologically representative ticks, 9 were identified by molecular methods as *H. rufipes* and 1 as *H. marginatum* s.s. (*6*).

Ticks belonging to the *H. marginatum* complex are common in large parts of the African and Eurasian continents. The immature



- 1 Kuş üstündeki 3 kene PCR ile pozitif
- Virus S segmentine göre Afrika 3 clade (grup)

Lindeborg M. et al. Emerg Infect Dis 2012

KKKA yayılımında Göçmen kuşlar, Fas

DISPATCHES

Crimean-Congo Hemorrhagic Fever Virus in Ticks from Migratory Birds, Morocco[1]

Ana M. Palomar, Aránzazu Portillo, Paula Santibáñez, David Mazuelas, Juan Arizaga, Ariñe Crespo, Óscar Gutiérrez, Juan Francisco Cuadrado, and José A. Oteo

Figure 1. Location of Zouala, Morocco.

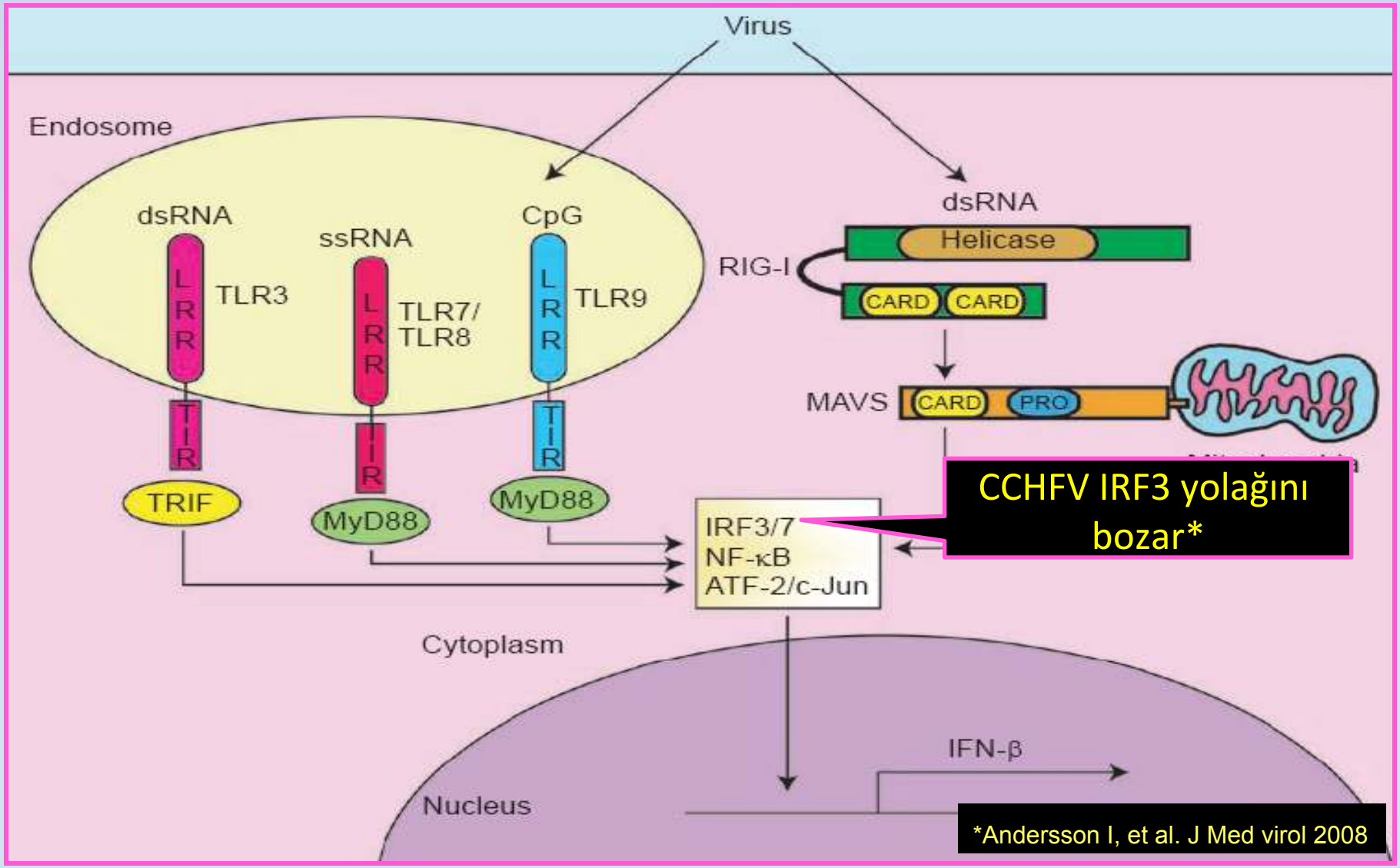
- 52 kene 6 havuzda toplanmış
- Tüm keneler Hyalomma
- 6 kene havuzundan 4'ü PCR ile CCHFV pozitif

Palomar AM. et al. Emerg Infect Dis 2013

KKKA Patogenezi

- Hala açık değil !
- Dendritik hücreler, endotel, monositler, makrofajlar, hepatositler, adrenal hücreleri ana hedef !
- İnflamatuar mediyatörler
  - IL-6, IL-8, IL-10, TNF-alfa, NO.....
- Koagülasyon fonksiyon defektleri, fibrinoliz
  - Peteşi, ekimoz, kanamalar
  - Yaygın damariçi pıhtılaşma (YDP)

İnterferon(IF) yanıtı



ELSEVIER

INSTITUT PASTEUR

Microbes and Infection 12 (2010) 1071–1078

www.elsevier.com/locate/micinf

Original article

Toll-like receptor 8 and 9 polymorphisms in Crimean-Congo hemorrhagic fever

Aynur Engin [a,*], Serdal Arslan [b], Sibel Kizildag [b], Hasret Oztürk [b], Nazif Elaldi [a], Ilyas Dökmetas [a], Mehmet Bakir [a]

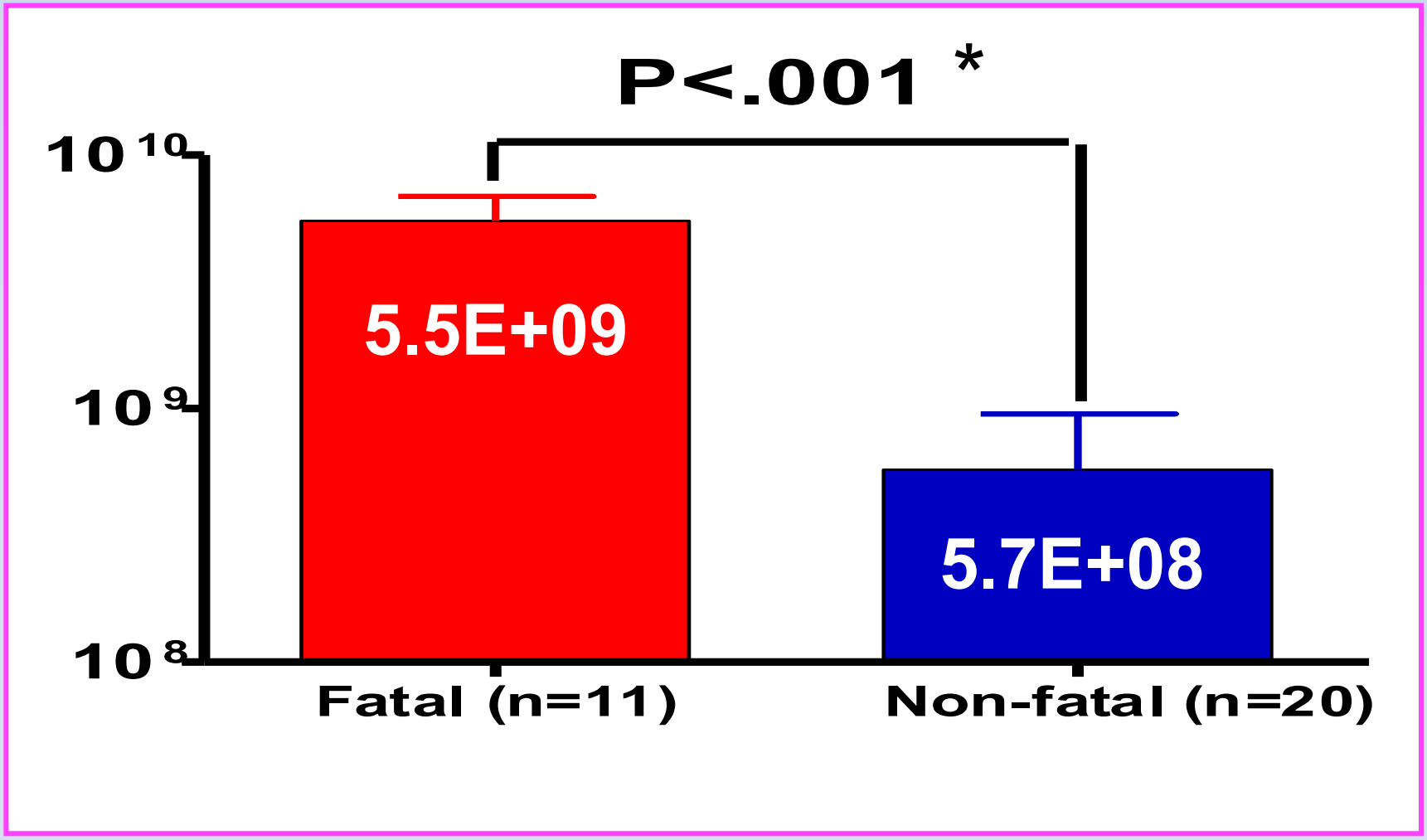
[a] *Departments of Infectious Diseases and Clinical Microbiology, Cumhuriyet University, School of Medicine, 58140 Sivas, Turkey*
[b] *Department of Molecular Biology and Genetics, Faculty of Science and Literature of Cumhuriyet University, 58140 Sivas, Turkey*

Received 12 June 2010; accepted 12 July 2010
Available online 30 July 2010

Abstract

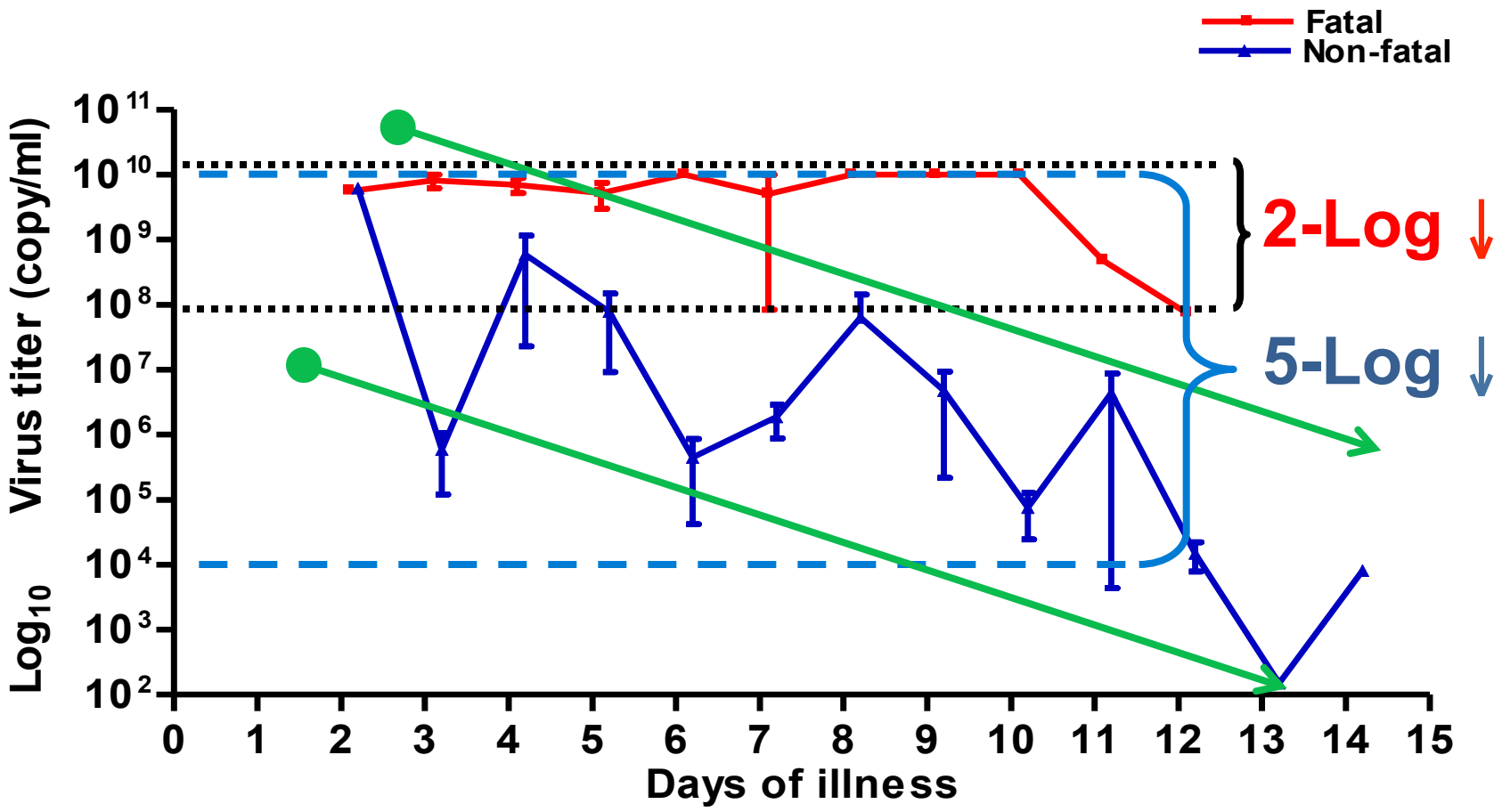
Crimean-Congo hemorrhagic fever (CCHF) is an acute viral hemorrhagic fever. The clinical course and outcome of the CCHF infection are different in humans. Toll-like receptors (TLRs) are a family of pathogen recognition receptors. TLR8 and TLR9 contribute to the recognition of viruses. We investigated frequency of *TLR8* Met1Val, *TLR8* -129C/G, *TLR9* -1486T/C and *TLR9* 2458G/A polymorphisms in CCHF patients and healthy controls. Our study was conducted between June 1 and August 31, 2007 in Cumhuriyet University Hospital, Turkey. TLR genotypes were detected using the PCR-RFLP assay in 85 CCHF patients and 171 healthy controls. We found that heterozygous plus homozygous mutant genotypes frequency for *TLR8* Met1Val and for *TLR9* -1486T/C were significantly higher in CCHF patients than controls ($p = 0.038$ and $p = 0.009$, respectively). The frequency of *TLR8* -129G/G genotype in the fatal CCHF patients was significantly higher than that of the non-fatal patients ($p = 0.026$). The frequency of *TLR9* -1486C/C genotype was significantly higher in fatal CCHF patients than in healthy controls ($p = 0.009$) and in patients with severe disease compared to non-severe disease ($p = 0.044$). Our findings suggest that *TLR8* Met1Val, *TLR8* -129C/G, and *TLR9* -1486T/C polymorphisms are important on clinical course of CCHF disease.

Hastaneye başvuruda virüs yükü



*Kaya S, Elaldi N, et al. BMC Infect Dis, 2014

Serum CCHF virüs kinetiği



*Kaya S, Elaldi N, et al. BMC Infect Dis, 2014

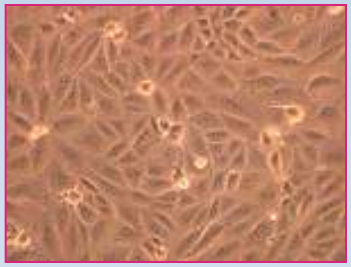
KKKA'da ölüm ile bağlantılı

- Kontrol edilemeyen viremi
- Özgül IgG antikor yokluğu
- ↑ Sitokin seviyeleri
- Yaygın damariçi pıhtılaşma
  - Kanamalar
- ŞOK

ÖLÜM

KKKA'da Özgül Tanı

- Kan örneklerinden virus izolasyonu
  - –Fare beynine inokulasyon
  - –Hücre kültürü (Vero E6, BHK 21, SW 13)
- Moleküler tanı yöntemleri
  - –RT-PCR (nested)
  - –Real time-PCR
- Serum örneklerinden antikor tayini
  - •ELISA IgM
  - •ELISA IgG
  - •IFA
  - •Pasif hemaglutinasyon inhibisyon
  - •İmmunofluoresan
  - •Nötralizasyon
  - •Kompleman fiksasyon
  - •İmmünodifüzyon



KKKA Kliniği

İnkübasyon periyodu

- Kene tutunmasından sonra

  -1-3 (En fazla 9) gün

- İnfekte kan/doku teması sonrası

  -3-10 (En fazla 13) gün

Belirtiler

Ani başlangıçlı

- Baş ağrısı
- Üşüme-titreme
- Ateş
- Kas ağrıları
- Baş dönmesi
- Boyun ağrısı
- Bel ağrısı

Belirtiler

- Yaygın karın ağrısı
- Göz dibinde ağrı
- Fotofobi
- Bulantı
- Kusma
- İshal

Kliniği ağır hastalarda

- Birkaç gün sonra

  -Şuur bulanıklığı

  -Huzursuzluk

  -Uyuma hali

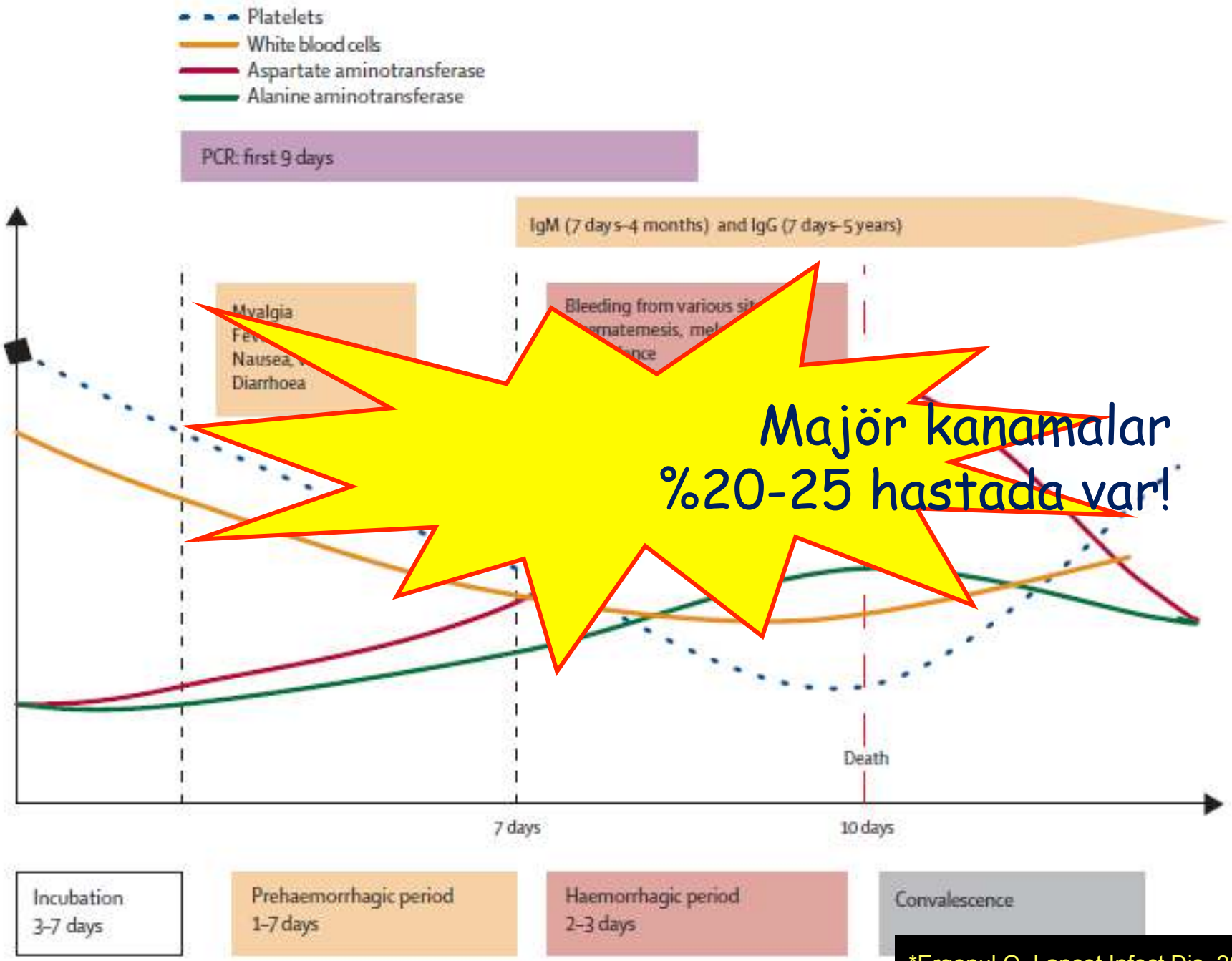
  -Çöküntü hali

  -Bezginlik

  -Karaciğer lojunda ağrı

Terminal dönemde

- Koma
- Şok
- Multiple organ yetmezliği
- Ölüm

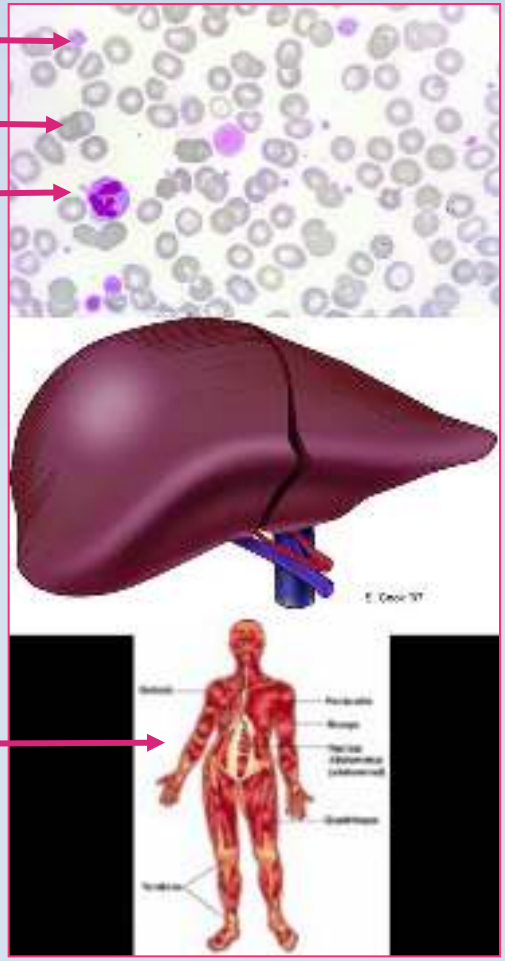


*Ergonul O, Lancet Infect Dis, 2006

Laboratuvar bulguları

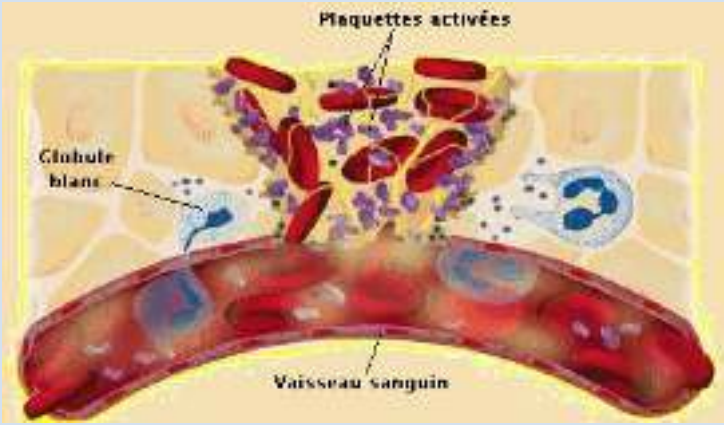
- Trombositopeni
- Anemi
- Lökopeni
- Lökositoz
- AST ↑
- ALT ↑
- GGT ↑
- ALP ↑
- LDH ↑

- CPK ↑
- BUN ↑
- Kreatinin ↑
- Proteinüri
- Hematüri



Laboratuvar bulguları

- Koagülasyon fonksiyon testlerinde bozulma
  - -PT ↑
  - -aPTT ↑
  - -INR ↑
  - -D-dimer ↑
  - -Fibrinojen ↓



KKKA Tedavisi

- Destek tedavisi
- Ribavirin tedavisi ?
- Bağışık serum tedavisi ?
- Diğer tedaviler ?

Destek tedavisi

1- Sıvı ve elektrolit takibi

2- Koagülopati takibi… Gerekliyse;

-TDP -Trombosit aferezi

3- Kanama takibi…..Gerekliyse;

-Tam kan/Eritrosit suspansiyonu

4- Gerektiğinde Yoğun Bakım Ünitesi'nde takip

Ribavirin ile klinik çalışmalar

Araştırıcı Adı	Yıl	Form	Hasta sayısı ribavirin/kontrol	Mortalite
Mardani M.	2003	PO	139/48	↓ ↓
Ergönül Ö.	2004	PO	8/22	⟷
Alavi-Naini	2006	PO	236/19	↓ ↓
Özkurt Z.	2006	PO	22/38	⟷
Çevik M.A.	2008	IV	9/16	⟷
Fışgın N.	2009	PO	21/20/11	⟷
Elaldı N.	2009	PO	126/92	⟷
Köksal İ.	2010	PO	64/72	⟷

KKKA tedavisinde ribavirin: Sivas deneyimi

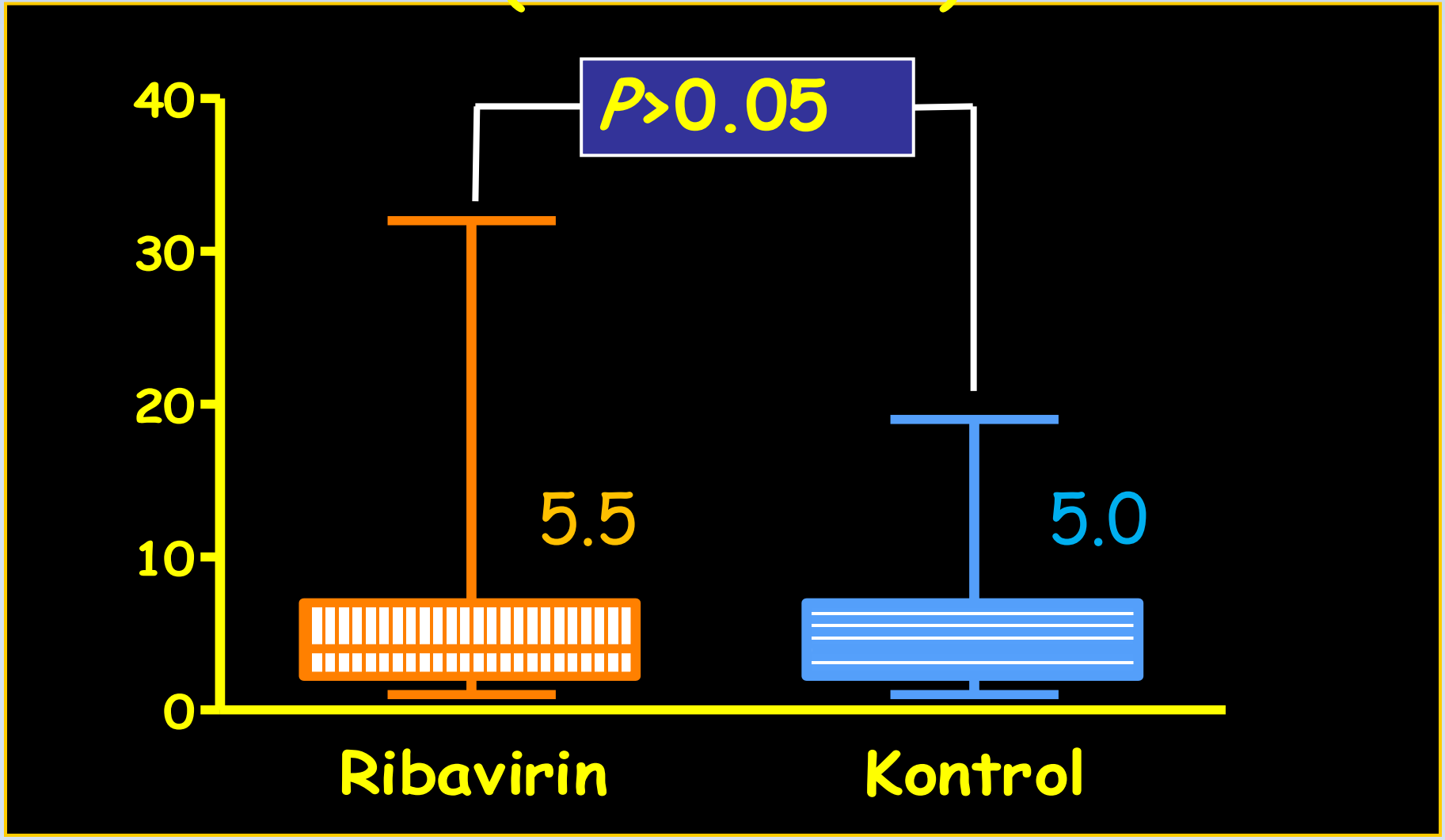
- 2003-2009 yılları arasında yatan konfirme KKKA hastaları
- Geriye dönük kohort
- İki gurup hasta
  - **Oral ribavirin alanlar (Ribavirin gurubu)**
  - **Oral ribavirin almayanlar (Kontrol gurubu)**

KKKA'da Oral ribavirin etkisi

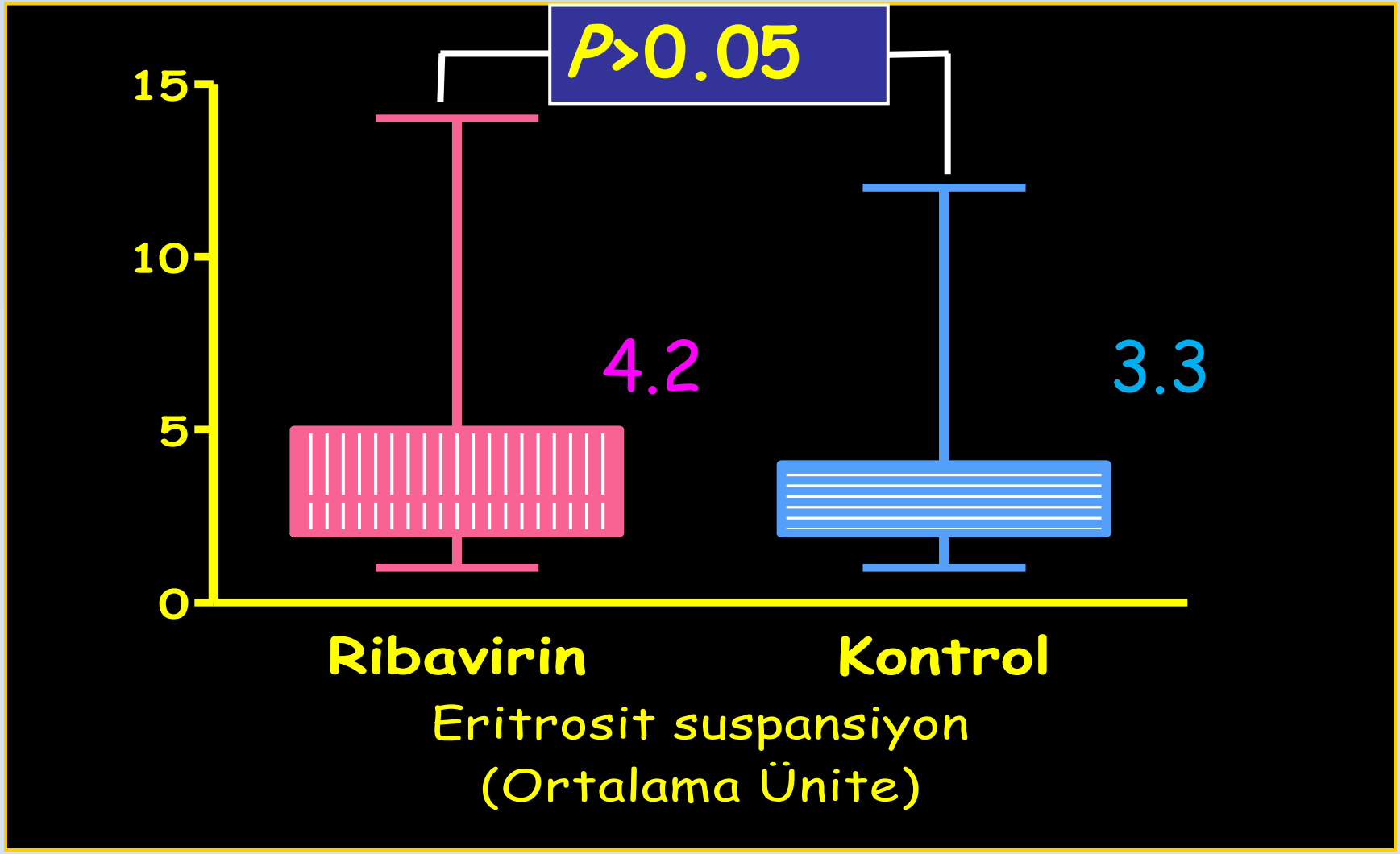
	Ribavirin (n=328)	Kontrol (n=506)	P-değeri
Ölen, *n*(%)	24 *(7.1)*	36 *(7.0)*	**0.938**
Yaşayan, *n*(%)	312 *(92.9)*	478 *(93.0)*	

***P*>0.05**

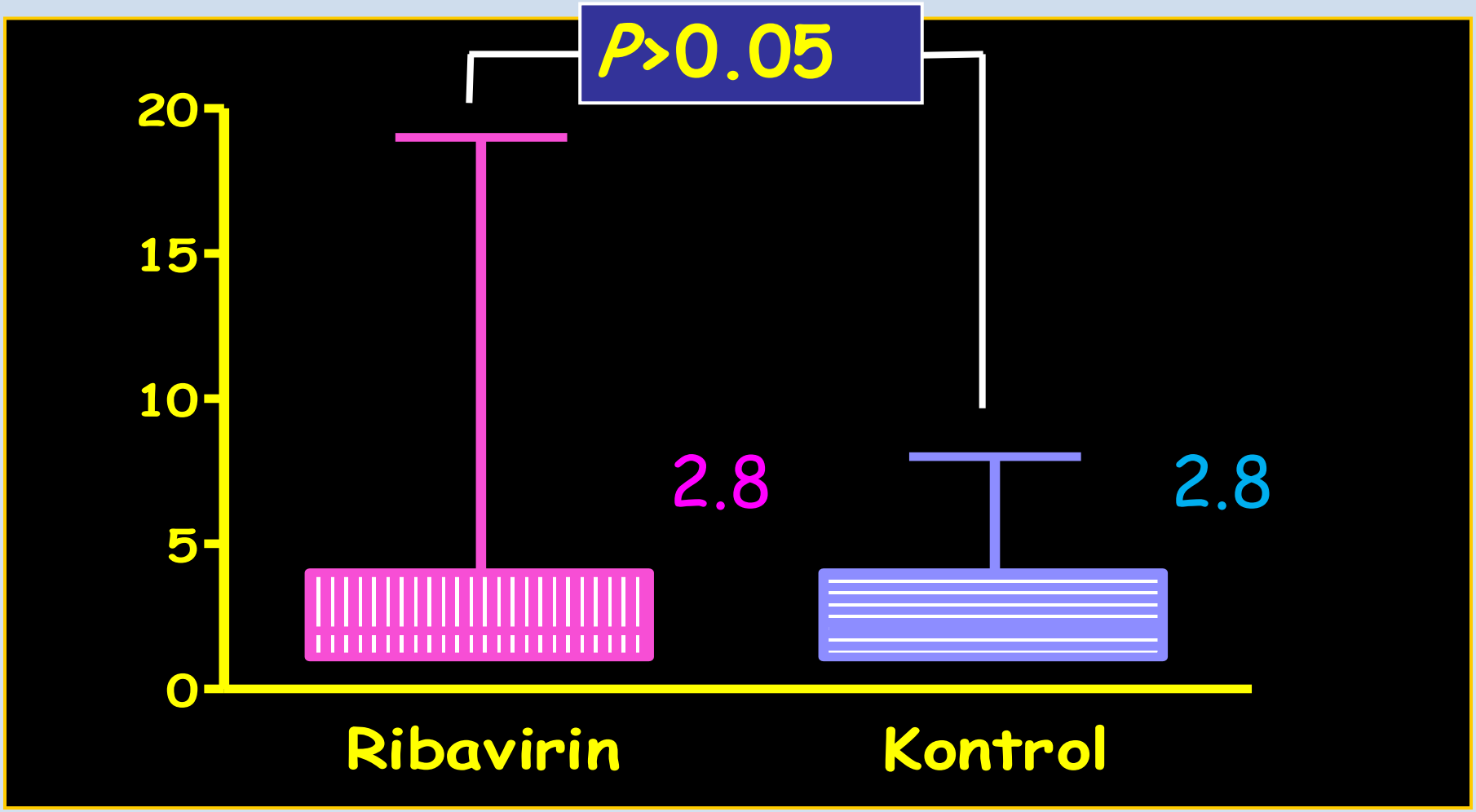
Uygulanan Taze Donmuş Plazma (Ort. Ünite)



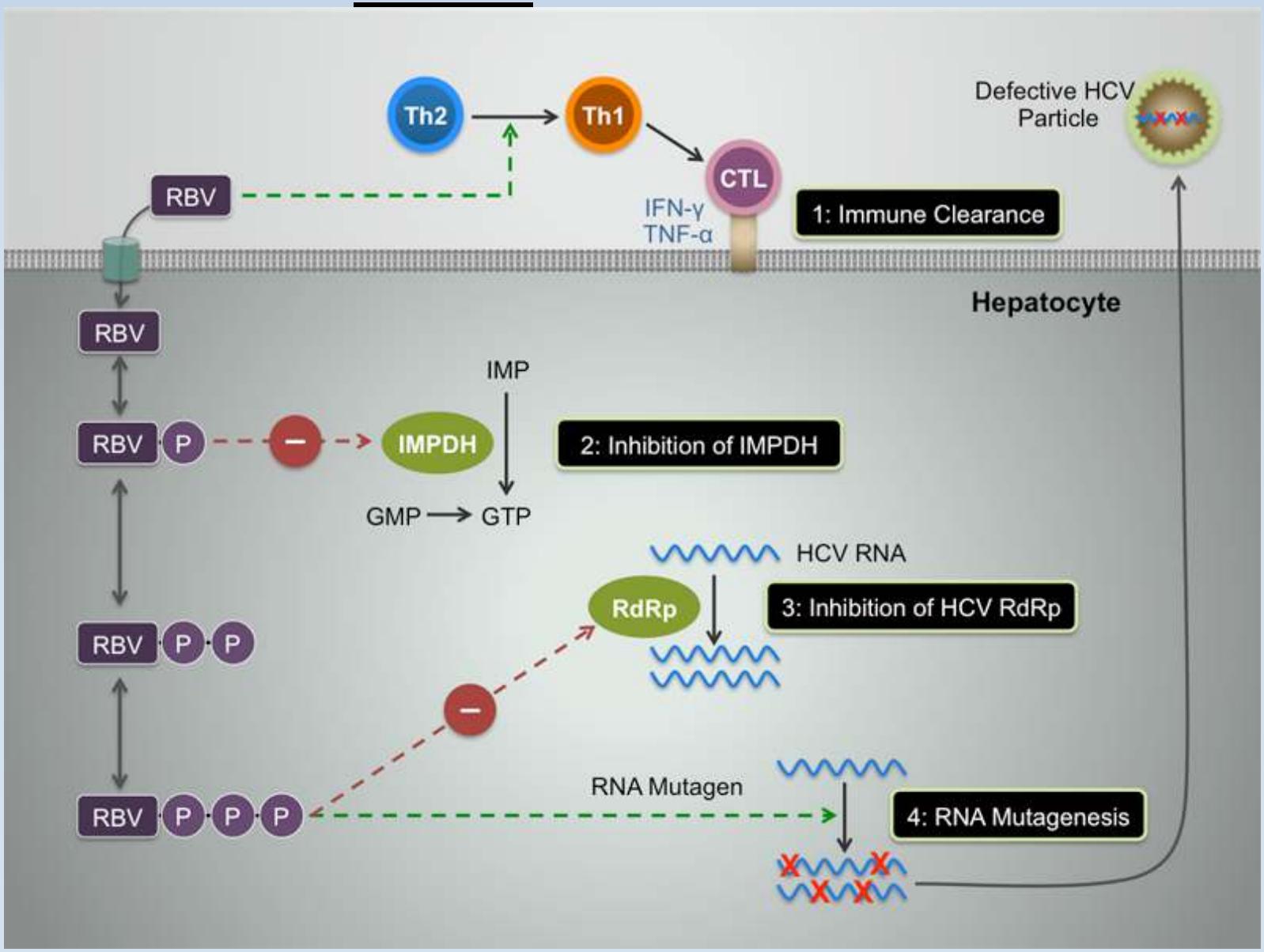
Uygulanan Eritrosit Süspansiyonu (Ort. Ünite)



Uygulanan Platelet süspansiyonu (Ort. aferez Ünite)



Ribavirin olası etki mekanizmaları



Favipiravir (T705)

OPEN ACCESS Freely available online

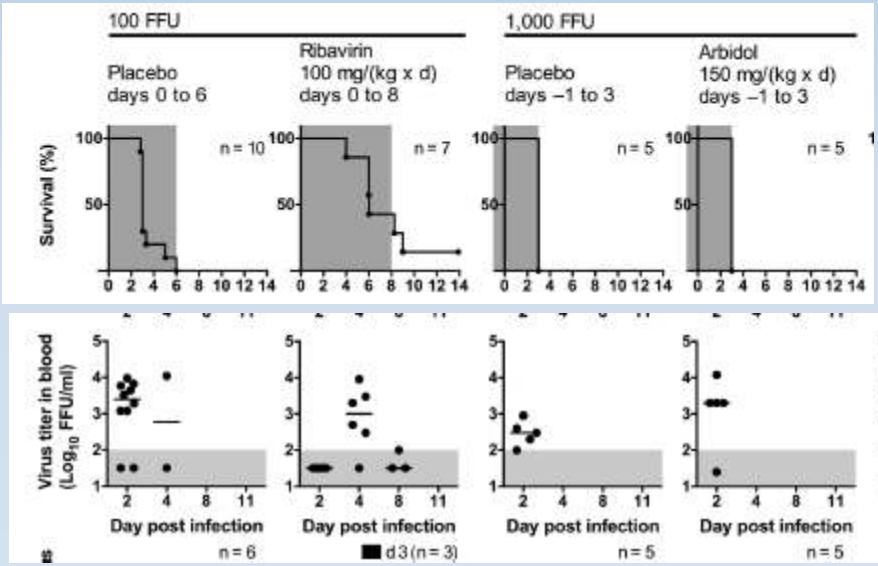
PLOS | NEGLECTED TROPICAL DISEASES

Evaluation of Antiviral Efficacy of Ribavirin, Arbidol, and T-705 (Favipiravir) in a Mouse Model for Crimean-Congo Hemorrhagic Fever

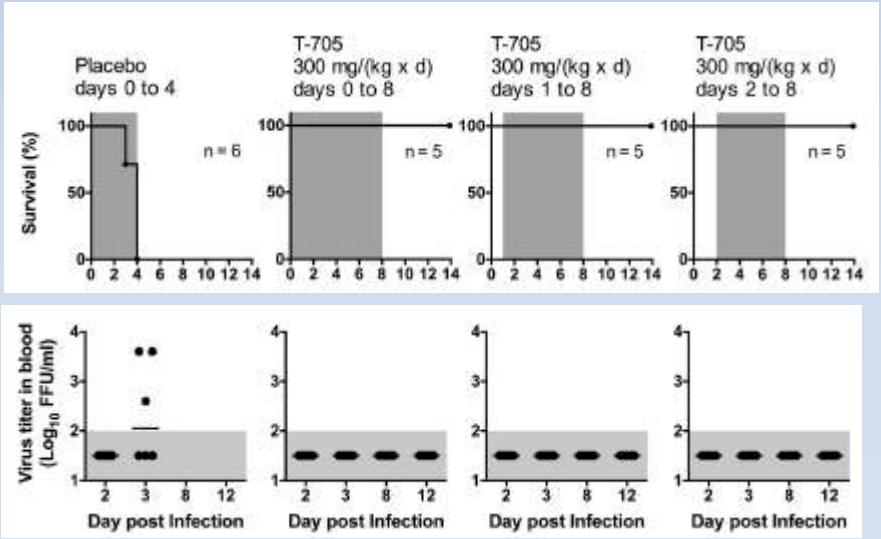
Lisa Oestereich[1,2☯], Toni Rieger[1,2☯], Melanie Neumann[3], Christian Bernreuther[4], Maria Lehmann[1,2], Susanne Krasemann[3], Stephanie Wurr[1,2], Petra Emmerich[1,2], Xavier de Lamballerie[5], Stephan Ölschläger[1¶¤], Stephan Günther[1,2¶*]

1 Department of Virology, Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany, **2** German Centre for Infection Research (DZIF), Hamburg, Germany, **3** Mouse Pathology Core Facility, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, **4** Institute of Neuropathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, **5** Aix Marseille Université, IRD French Institute of Research for Development, EHESP French School of Public Health, UMR_D 190 "Emergence des Pathologies Virales", Marseille, France

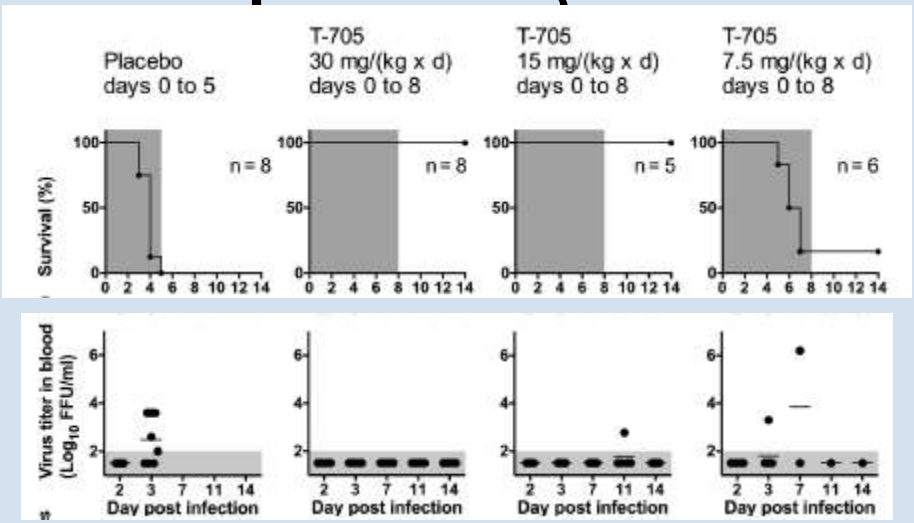
Ribavirin ve Arbidol



Favipiravir 300 mg/Kg



Favipiravir düşük doz




Teşekkür ederim!